REMARKS

Claims 1-8, 55-58, and 63 were pending. Claims 2 and 7 have been cancelled. Claim 1, 3-6, 8, 55, and 63 were amended. Claims 64-68 were added. Therefore, claims 1, 3-6, 8, 55-58, and 63-68 will be pending upon entry of the present amendment.

No new matter has been added. Support for the amendments to claim 1 can be found in the specification as originally filed, for example, at least at, page 8, lines 28-37, page 9, lines 19-21 and page 55, line 30. Claims 3-6 and 8 were amended to clarify the invention. Support for the amendment to claim 55 can be found, for example, in the specification as originally filed, at least at page 8, lines 19 and 28-37 and page 9, lines 19-21. Support for the amendments to claim 63 can be found, for example, at least at page 8, lines 28-37 and page 9, lines 19-21. Support for new claim 64 can be found in the specification as originally filed, at least at claim 1 and at page 14, line 24 though page 15, line 4. Support for new claim 65 can be found in the specification as originally filed, at least at page 14, line 35. Support for new claim 66 can be found, for example, at least at in claim 1 as originally filed, page 8, lines 28-37, page 9, lines 19-21 and page 17, line 29. Support for new claims 67 and 68 can be found in the specification as originally filed, for example, at least at page 8, lines 28-37 and page 9, lines 19-21.

Rejection of Claims 1, 3-6, 8, 55-58 and 63 under 35 U.S.C. § 112, first paragraph

Claims 1, 3-6, 8, 55-58 and 63 are rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for 2D and 3D geometrically ordered structures, does not reasonably provide enablement for the formation of any arbitrarily chosen ordered structure."

Applicant disagrees. However, in the interest of expediting prosecution, Applicant has amended the claims to recite that the ordered structure is a two- or three-dimensional ordered array of the amphiphilic molecules. Applicant submits that the present scope of the claimed invention fully enables one of ordinary skill in the art to make and use the full scope of the claimed invention.

Therefore, Applicant respectfully requests that this rejection of claims 1, 3-6, 8, 55-58. and 63 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejection of Claim 6 under 35 U.S.C. § 112, second paragraph

Claim 6 was rejected under 35 U.S.C. § 112, second paragraph, for "being indefinite for failing to particularly point out and distinctly claim the invention." In particular, the Examiner rejected claim 6 for the recitation of "said proteins" in line 1.

Applicants respectfully submit that this rejection no longer applies to claim 6 as currently amended and request that this rejection be withdrawn.

Rejection of Claims 1-8, 55-58, and 63 under 35 U.S.C. § 101

Claims 1-8, 55-58, and 63 were rejected under 35 U.S.C. § 101, because the Examiner found that the "claimed invention lacks patentable utility." Claims 2 and 7 have been cancelled, thus rendering their rejection moot.

Applicants disagree for at least the following reasons. Applicant's methods of making two and three dimensional ordered arrays are useful because they offer a novel method of obtaining both functional and structural information about the amphiphilic molecule that is being analyzed and its interactions with other molecules. The claimed methods are fast (several minutes vs. days and months using conventional techniques) and require only a small amount of material (a fraction of a milligram vs. grams of the amphiphilic molecules required by convention techniques). In addition, the methods of the present invention allow the amphiphilic molecules to be ordered in their natural environment without using detergents or solubilizing agents. In contrast to conventional techniques which solubilize or reconsistitute the amphiphilic molecules, the methods of the present invention allow amphiphilic molecules to retain its function as well as its native conformational state, than it would in a solubilized or reconstituted form. Furthermore, the methods of the invention do not require the use of a highly purified protein. Instead, the claimed methods can be used to form ordered structures of amphiphilic molecules, such as proteins, from small quantities of a crude preparations, such as crude membrane preparations. This is of considerable advantage for membrane proteins, since most membrane proteins are not readily available in large quantities and it is even more difficult to find them in a purified form. The methods of the present invention overcome the limitations imposed by conventional methods. The methods of the invention have the potential to be adopted as a general means to produce ordered structures of amphiphilic molecules, such as membrane proteins, in a fast and cost-effective manner.

Therefore, Applicant submits that the claimed process is both new and useful and respectfully requests that this rejection of the claims under 35 U.S.C. § 101 be withdrawn.

Rejection of Claims 1-6, and 8 under 35 U.S.C. § 102(b)

Claims 1-6 and 8 were rejected under 35 U.S.C. § 102(b) as being unpatentable over Verclas *et al.* (*J. Mol. Biol.*, (1999) 287, 837-843). Claim2 has been cancelled, thus rendering its rejection moot.

Applicant claims a method for forming a two- dimensional ordered crystalline structure of proteins. The method includes contacting a population of proteins with a interface; and laterally compressing the population to an appropriate pressure, such that a two- dimensional ordered crystalline structure of the proteins is formed at the interface. Applicant's two-dimensional ordered crystalline structures of proteins have a diameter of greater than 25 μm.

Verclas *et al.* describe a method for obtaining X-ray diffraction data from a single layer of purple membrane on an air-water interface. Verclas *et al.*'s method describes small "crystallites" of purple membrane at all pressures including $\Pi=0$. It is known in the art that purple membrane is comprised of high concentrations (>95%) of bacteriorhodopsin, which are already packed in two-dimensional crystallites. As a result, the crystallites observed by Verclas *et al.*, are likely due to the presence of these inherent 2D crystallites, rather than formed by the methods described by Verclas *et al.* In contrast to Applicant ordered two-dimensional crystalline structures which can have diameters of 25 μm and greater. Verclas *et al.* report that their crystallites are very small - 300-500 nm (page 839, left column, line 19).

As described above, Applicant's claimed methods for the formation of two dimensional ordered structures require the use of lateral compression. While Verclas *et al.* describe altering the amount of membrane protein by altering the salinity of the preparation, Verclas *et al.* does not teach or suggest the lateral compression to form a two-dimensional crystalline ordered structure of proteins. Verclas *et al.* fails to teach or suggest Applicant's claimed method of laterally compressing a population of proteins to form two dimensional ordered crystalline structure, as claimed by Applicant. Furthermore, Verclas *et al.* fails to teach or suggest large (e.g., greater than 25 μm in diameter) ordered crystalline structures of proteins, as claimed by Applicant.

Therefore, Applicant respectfully requests that this rejection of claims 1, 2-6 and 8 under 35 U.S.C. § 102(b) be withdrawn.

Rejection of Claim 7 under 35 U.S.C. § 103(a)

Claim 7 was rejected under 35 U.S.C. § 103 (a) as being unpatentable over Verclas *et al.* in view of Hemming *et al.* (JMB (1995) 246, 308-316) and in further view of Koppenol *et al.* (*J. of Pharmaceutical Sci.*, Vol. 86, 11:1997). Claim 7 has been cancelled, thus rendering its rejection moot.

Rejection of Claims 55-57 under 35 U.S.C. § 103(a)

Claims 55-57 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Verclas *et al.* in view of Hohenfeld *et al.* (FEBS Letters 442 (1999) 198-202) and in further view of Koppenol *et al.* (*J. of Pharmaceutical Sci.*, Vol. 86, 11:1997).

Claim 55 and its dependent claims are directed to a method for fabricating a two- or three- dimensional ordered crystalline structure of a protein. The method includes expressing the protein in a cell; obtaining the protein from the cell; applying the protein to an interface in a crude membrane preparation; and compressing the protein on the interface to an appropriate pressure, such that a two- or three-dimensional ordered crystalline structure of the protein is formed.

The disclosure of Verclas *et al.* has been described above. In addition, it is noted that the method described by Verclas *et al.* requires the delipidation of the purple membrane proteins (page 838, right column, lines 17 to 19). Verclas *et al.* does not teach or suggest methods for making ordered crystalline structures of proteins using crude membrane preparations, as claimed by Applicant. In contrast, Verclas *et al.* teaches away from the present invention by purifying the membrane proteins before attempting to make the purple membrane monolayers.

The secondary references, Hohenfeld *et al.* and Koppenol *et al.*, fail to over come the deficiency of the primary reference. Hohenfeld *et al.* is directed to the expression of non-native proteins in *E. coli*. Koppenol *et al.* also teaches away from the present invention by stating that having a high concentration of the protein at the interface is important to two-dimensional protein crystal formation. Each of Hohenfeld *et al.* and Koppenol *et al.*, alone or in combination, fail to overcome the deficiencies of Verclas *et al.* Therefore, Applicants respectfully request that this rejection of claims 55-57 under 35 U.S.C. § 103 (a) be withdrawn.

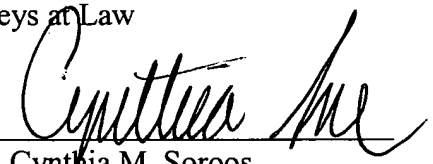
SUMMARY

The cancellation of and/or amendment to claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of/amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicant reserves the option to further prosecute the same or similar claims in the present or another patent application. The cancellation of and/or amendments to claims herein are not related to any issues of patentability.

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicant's Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Date: September 30, 2005

LAHIVE & COCKFIELD, LLP
Attorneys at Law

By 

Cynthia M. Soroos
Reg. No. 53,623
28 State Street
Boston, MA 02109
(617) 227-7400
(617) 742-4214